

SEARCHING, APPRAISING AND STORING

Birds feed their young by bringing back a tasty morsel like a worm or by swallowing and pre-digesting the food into a nutritious pap. Both have the objective of ensuring that the chick survives and grows and develops to fend for itself.

Bandolier aims to bring its readers both tasty morsels and pre-digested evidence. The evidence is sometimes positive, but occasionally negative. This issue contains a number of good solid negative pieces of evidence, which are often the most difficult to have published. Archie Cochrane wrote that evidence from randomised controlled trials would result in "a marked reduction in the use of ineffective remedies and of effective remedies used ineffectively."

Bandolier also hopes to do more to help its readers develop techniques for them to become more critical and therefore better informed practitioners of evidence-based health care.

SAS techniques

To be a lifelong learner requires the ability to learn the SAS techniques - searching, appraising and storing. In *Bandolier* we concentrate on appraisal techniques, either by showing examples of good appraisal articles or, in the Mindstretcher series, by concentrating on articles on methodology. Desert Island Texts, the first of which appears in this edition of *Bandolier*, is also focused on methodology of appraisal through highlighting landmark articles.

We will also carry articles on searching techniques and working with librarians, for modern librarians are the professional searchers, and on storing, giving advice on techniques that could be used to store references. We will be unashamedly advocating electronic storage systems because that is the only way practitioners of evidence-based health care can keep on top of the evidence base.

Writing for *Bandolier*

SAS methods will permeate *Bandolier* for the next year and we welcome articles from readers on these topics. We also welcome contributions to Desert Island Texts, and we will be awarding authors of published contributions a copy of the beautifully produced BMJ edition of Archie Cochrane's classic on effectiveness and efficiency.

FALSE POSITIVE EXPLOSION

Any diagnostic test has to be assessed with respect to its sensitivity - the proportion of cases it picks up - and its specificity - the proportion of people without the condition who are confirmed as normal. With the continuing progress of technology it is only to be expected that new diagnostic tests are becoming more sensitive, and most diagnostic tests, be they laboratory or imaging, emphasise sensitivity as an important selling point.

There are, however, few diagnostic tests which can discriminate absolutely between healthy and sick populations (that is have a specificity of 100%). For the individual tested, and for the Health Service, the specificity of any diagnostic test is probably more important.

As the number of tests inexorably increases, we are seeing an explosion of false positive tests. *Bandolier* will be carrying articles on false positives in future, but in this edition we focus on two types of false positives with imaging.

Perils of false positives

For the individual, being falsely diagnosed as having a disease can cause tremendous suffering which is not always easily set aside. For the Health Service, the generation of many false positives places increasing burdens on overstretched resources, resources which, in the end, are wasted.

False positives cause problems for patients, doctors and the Health Service because the GP who elicits a false positive biochemical test will almost certainly have to take some further action.

Most test results do not fall conveniently into simple yes/no answers with obvious and huge differences. Normal and abnormal values overlap, particularly with effects of age and medicaments. Definition of a "positive" is often set by using the upper 95th centile of a population as a cut off. This defines 5% of the population as being "abnormal" or "positive" - but it ain't necessarily so!

Just recently the Association of Clinical Biochemists and BUPA have produced a short handbook [1] on expected values for standard laboratory tests. Looking at tens of thousands of people, the results are given by age and sex, and colour coded so that the meaning of any result can quickly be obtained.

Thus a "high" alkaline phosphatase in a 30-year old man may have much more importance than the same result in a 75-year old woman.

This booklet is worth having handy when interpreting laboratory results.

The incidentaloma

A fascinating study from the *Annals of Internal Medicine* demonstrated just how commonly a pituitary adenoma could be diagnosed among normal people having an MRI scan. Scans were performed on 100 normal volunteers (70 women, 30 men, aged 18 to 60 years) before and after administration of paramagnetic contrast agent.

MRI scans from volunteers were mixed randomly with those of 57 patients with Cushing's disease, and all the scans were interpreted independently by three blinded and experienced reviewers.

Ten percent of normal volunteers were judged to have pituitary adenomas by two of the three reviewers (they had no pituitary endocrine disease). It is important to know that 10% of the normal adult population has pituitary abnormalities on MRI scanning, and that must be remembered when diagnosing pituitary disease - the positive predictive value of identification of a pituitary adenoma in patients with Cushing's disease was 86%. Between one and two patients with Cushing's syndrome and a pituitary adenoma identified by MRI scanning may not have Cushing's disease.

False positive slipped discs

Eight out of ten individuals will have low back pain at some time in their lives, and at any given time there are probably hundreds of thousands of patients suffering back pain in the UK. The costs of this, both to the Health Service and to society in general is huge.

How back pain is related to abnormalities in the lumbar spine is an area of controversy, but it is difficult to ignore a radiological abnormality in such a patient.

A paper in the *New England Journal of Medicine* suggests that ignoring such a finding may be in order. MRI examinations were performed on 98 asymptomatic people (50 men and 48 women aged 20 to 80 years); those with a history of back pain lasting more than 48 hours, or lower back problems were excluded.

These 'normal' MRI scans were mixed with 27 abnormal scans from patients with back pain, and all the scans were then evaluated blind by two experienced neuroradiologists. The readers independently evaluated the status of the five intervertebral disks in the lumbosacral spine in all 125 subjects.

The results showed that only 36% of the 98 asymptomatic subjects had normal disks at all levels. With the results of the two readings averaged, 52% had a bulge at least one level, 27% had a protrusion and 1% an extrusion. More than one disk was involved in 38% of people.

Thus MRI scans showed that "abnormal" pathology was the norm. An accompanying editorial [4] states laconically

that "the recent increase in the rates of lumbar spine surgery may be related in part to the availability of new imaging techniques".

False positive explosion

Increasing power to test may not only serve to increase sensitivity, but may also decrease specificity, create false positives and thus anxiety and unnecessary cost. *Bandolier* will be happy to share any experiences readers have of the false positive explosion.

References:

- 1 TP Whitehead, D Robinson, AC Hale, AR Bailey. Clinical Chemistry & Haematology - adult reference values. BUPA Medical Research, London, 1994.
- 2 WA Hall, MG Luciano, JL Doppman, NJ Patronas, EH Oldfield. Pituitary magnetic resonance imaging in normal human volunteers: occult adenomas in the general population. *Annals of Internal Medicine* 1994 120: 817-20.
- 3 MC Jensen, MN Brant-Zawadki, N Obuchowski, MT Modic, D Malakasian, JS Ross. Magnetic resonance imaging of the lumbar spine in people without back pain. *New England Journal of Medicine* 1994 331: 69-73.
- 4 Editorial: Magnetic resonance imaging of the lumbar spine. Terrific test or tar baby? *New England Journal of Medicine* 1994 331: 115-6.

LEG ULCERS

A REVIEW OF RESEARCH IN NURSING MANAGEMENT IN THE COMMUNITY

A detailed review of this important subject, commissioned by the Department of Health, has been conducted by Dr Nicky Cullum of the Department of Nursing in Liverpool [1]. This is an important and common disorder, and Nicky Cullum's review should be read by those treating leg ulcers in the community, especially nurses. It is easy to read, thorough and is a statement not only of where we are now, but also outlines the research agenda and research methods which should be used to make progress.

The two objectives of the report were:-

- To critically review the research-based information which underpins the nursing management of leg ulcer patients in the community.
- To highlight those areas where further research and development is required to inform nursing practice.

What are leg ulcers?

The best definition is that a leg ulcer is tissue breakdown on the leg or foot due to any cause. They occur in associa-

tion with a range of disease processes, most commonly with venous and/or arterial disease.

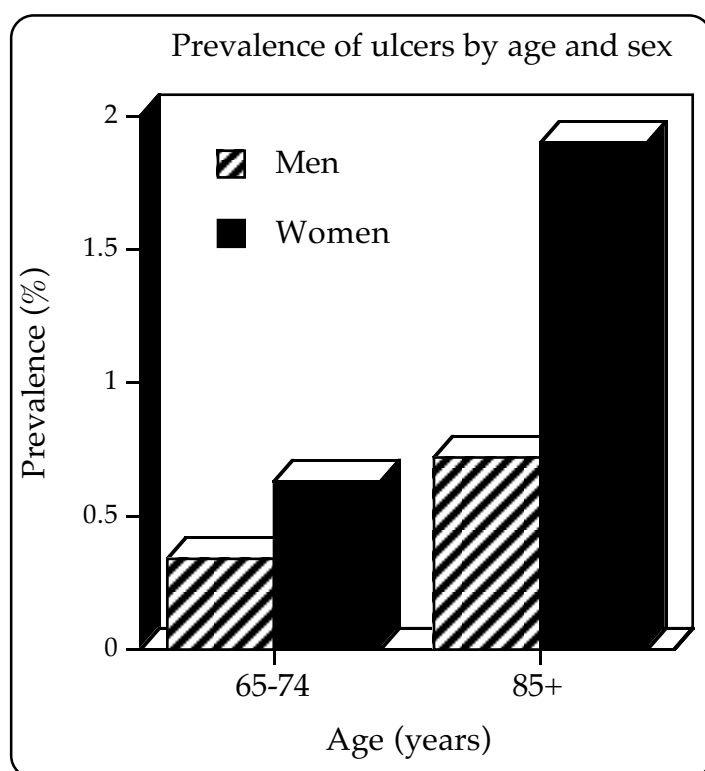
Those of venous origin are associated with venous hypertension arising from venous damage. How venous hypertension is translated into full-thickness skin defects is not clear, though fibrin deposits, decreased fibrin breakdown and white cell accumulation have been implicated.

Leg ulcers occur in patients with rheumatoid arthritis and diabetes, and may occasionally be self-inflicted either inadvertently or deliberately. What part nutritional or biochemical factors contribute to leg ulcers is not clear.

How big is the problem?

Two major studies in the UK have provided similar figures for the prevalence of active ulceration at 0.15 - 0.18%; that is 450 patients per health district of 250,000 population and 100,000 patients in the UK. Risk factors for leg ulcers are increasing age, female sex and venous disease.

The graph shows the increasing prevalence of leg ulcers in over 65s. The prevalence of a *history* of leg ulcers in this population was 3.6%, suggesting that only 20-25% of ulcers are open at any time. It has been suggested that nearly 1% of the population may be affected by leg ulceration at some time during their lives.



Leg ulcers seem to have a typical cycle of healing followed by re-ulceration and re-healing. In surveys, two-thirds of patients with leg ulcers were already experiencing a recurrence, and a third had experienced four or more episodes of ulceration.

When the ulcers are open, they tend to be present for some time. In cross-sectional surveys, half of all ulcers had been open for 9 - 12 months, 20% open for two years and 8% open for over five years.

Leg ulcers begin before the age of 40 years in 22% of those affected, and a significant minority (18%) were in full-time employment; in these patients, earning capacity was affected in 40%.

How is leg ulcer treatment organised?

Although delivery of care varies, between 60% and 90% of patients are managed entirely in the community. District Nurses are mainly responsible for the delivery of leg ulcer care along with Practice Nurses; fewer than 10% of patients are managed in hospital clinics. Some 8% - 22% of District Nurses' caseload comprises leg ulcer treatment.

There is a little evidence to show whether differences in health care delivery can improve leg ulcer healing, but there are suggestions that District Nurses' expectations of ulcer healing are low.

What is the cost of treating leg ulcers?

There are few reports, and the bases for costings are not explicit. The best estimate of the total cost in the late 1980s was £100-£120 million a year; other estimates have ranged up to £600 million a year.

Costs on an individual patient basis have ranged from £1100 to over £5000 per patient per year, but a figure of about £2000 per patient per year would appear to be more likely. Based on 100,000 patients in the UK, this would give an annual spend of £200 million.

Which treatments work?

Nicky Cullum's report has a 90-page chapter covering the evidence for the effectiveness of leg ulcer treatments. It covers the fundamentals of wound healing, the place of moisture and the rôle of oxygen in wound healing, the effects of pH and the use of antimicrobial therapies. The chapter also reviews debridement, compression bandaging and about 15 other treatments and issues, including relative esoterica like electricity and ulcer healing.

It is not possible to summarise here the results of all of the many studies examined for this report. However, certain points stand out:-

- No single treatment method stands out as having unsurpassed effectiveness.
- There are severe methodological problems with almost all of the studies reviewed.
- Contact sensitivity in patients with leg ulcers is a widespread problem; 50-85% of leg ulcer patients attending dermatology outpatients clinics demonstrate sensitivity to one or more allergens. Allergic reactions to lanolin, topical antibiotics, cetyl steryl alcohols, basalm of Peru and parabens may contribute to non-healing and cause discomfort to the patient.

Perhaps the best summary is that the key therapy for people with uncomplicated venous ulcers is compression bandages.

Despite this apparently negative conclusion, there is a wealth of detail in the report, and it provides a solid base of current knowledge for those involved in the treatment of patients with leg ulcers, or those who make policy.

More and better research needed

The review makes the point that so many of the studies conducted in leg ulcers are near worthless because of methodological flaws, not an uncommon experience for those engaged on systematic reviews. Dr Cullum, however, provides some light at the end of the tunnel not just by reciting all the aspects of leg ulcers which desperately need good research, but actually by telling us how that research should be conducted if it is to be of value. *Bandolier* makes no excuses for repeating them in the box.

Key Issues in Leg Ulcer Research

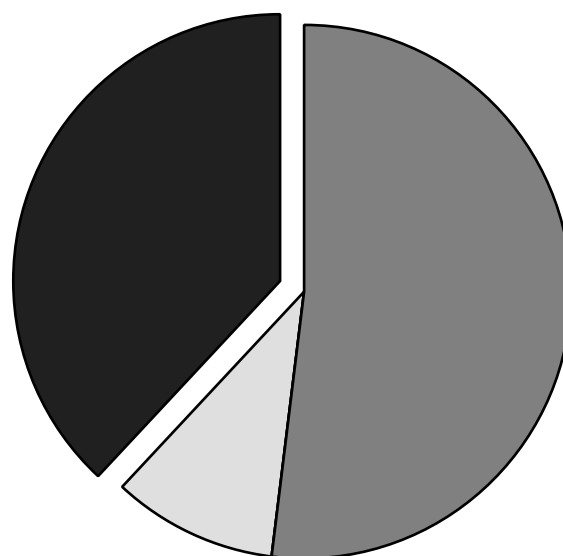
- Random allocation of intervention and control groups is mandatory.
- Prior calculation of sample sizes so that studies have adequate power to discriminate clinically important differences.
- Clear inclusion and exclusion criteria are needed.
- The choice of control treatment should be reasonable.
- Confounding variables (like levels of compression in bandaging) should be avoided by standardising common aspects of intervention and control groups.
- Trials should be of sufficient duration to demonstrate complete healing rates.
- All clinically relevant outcomes should be reported - including adverse events and how they are assessed and handled.
- If possible, details of arterial/venous status should be objective.
- All patients should be accounted for - the numbers and reasons for withdrawals should be explicit.
- Additional information, like patient comfort or satisfaction scores, frequency of dressing or bandage changes required, or differences in nursing time or frequency are useful in making assessments of the relative effectiveness of treatments.
- Measurement of ulcer size is important, and the report gives a good review of this.

RCT of aspirin for leg ulcers

Earlier this year saw the publication of a short report on this subject in *The Lancet* [2]. This trial fulfilled the majority of the features highlighted above, omitting only the prior calculation of power, and additional information. It was limited to four months, but complete ulcer healing was one outcome.

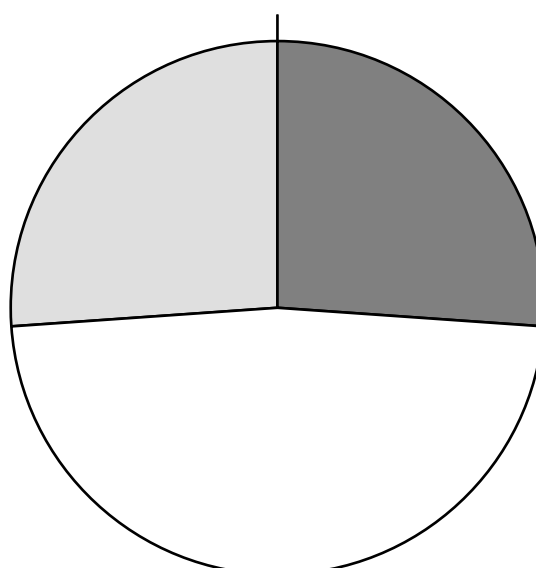
The study involved 20 patients attending dermatology outpatients with chronic venous leg ulcers over 2 cm diameter who were randomly allocated to treatment or control. The treatment was 300 mg of enteric-coated aspirin or identical placebo, one tablet daily.

300 mg Aspirin per day



■ Reduced size □ Same
■ Increased size ■ Healed

Placebo



aspirin, compared with none in the placebo group, and twice as many ulcers improved (smaller area) in those taking aspirin compared with placebo.

Although the numbers recruited in this study were small, and the power therefore was low, the differences between the groups was large. This study fulfilled most of the qualities required for research in leg ulcers, and aspirin looks as if it is a useful treatment applicable to a high proportion of patients with leg ulcers. Its use as a prophylactic against recurrence was not tested.

References:

- 1 N Cullum. The nursing management of leg ulcers in the community: a critical review of research. Available from Department of Nursing, University of Liverpool, PO Box 147, Liverpool L69 3BX.
- 2 AM Layton, SH Ibbotson, JA Davies, MJD Goodfield. Randomised trial of oral aspirin for chronic venous leg ulcers. *Lancet* 1994 344: 164-5.

PRESSURE SORES

A GOOD SOLID NEGATIVE FOR VITAMIN C AND ULTRASOUND

In a previous *Bandolier* (#6, July 1994) we reported on five reviews of pressure sores and an RCT of a pressure relieving bed which showed a very positive effect for that device. Like leg ulcers, a range of different treatments have been used to heal pressure sores, and amongst these vitamin C supplementation and ultrasound have been suggested.

We are delighted to have received a report of two more RCTs on these issues from Dr Gerben ter Riet, of the University of Limburg in Maastricht, working with Dr Paul Knipschild who is well known for his work on systematic reviews in healthcare.

The RCTs are contained in a published thesis which has an excellent review of the literature and extremely detailed trial design and reports on the validity of the models and practical problems faced in the conduct of this sort of study.

Vitamin C

Vitamin C has been thought of as being useful in pressure sore management, and the outline research results on which this was based were reported in *Bandolier* 6.

In this RCT, patients with pressure sores graded II, III or IV were recruited from nursing homes and a hospital in southern Holland. Patients with more than one ulcer had the worst chosen for inclusion, mainly those on the trunk. There

were a number of exclusion criteria, including patients already taking more than 50 mg of vitamin C supplementation a day and those who were unlikely to survive for the 12-week observation period.

Allocation of patients to active treatment or standard therapy was random, within a block design to ensure between group similarity. Active and placebo tablets were identical in colour, taste, disintegration time and friability, except that active medicine contained 500 mg ascorbic acid, while the placebo tablets contained only 10 mg. Tablets were taken twice daily. Topical wound care was mostly undertaken by the same doctor/nurse team.

Colour slides were taken of the wounds at the start and 1, 2, 4, 6, 8, 10 and 12 weeks, and pressure sore areas and volumes were measured. A number of effect measures were used, and subjective measures were made by independent assessors.

In 1991 and 1992, 88 patients were randomised. In the active treatment group, plasma vitamin C levels rose by 11.3 mg/L in the first two weeks, compared with 0.9 mg/L for the control group over the same period. Mean stable levels in the active group were about 15 mg/L compared with about 5 mg/L in the controls.

While there was comparability between the active and placebo groups, no difference was found in the rate of wound healing by any of the many parameters used to measure it.

While an absolute deficiency of vitamin C may delay wound healing, supplementation beyond 10 to 20 mg per day does not speed up healing.

Ultrasound

Part of Dr ter Riet's thesis concerned the beliefs of healthcare professionals in Holland concerning treatments thought to be effective for pressure sore healing. Ultrasound was thought to be effective by 20% of nursing home physicians and 25% of supervisory nurses; 50% of physicians and 33% of the nurses thought it was ineffective, so a clear disagreement over the place of ultrasound existed. Few RCTs have examined this.

The same criteria were used as for vitamin C above. The ultrasound protocol used was approved by a sample of Dutch education centres for physiotherapy, and patients were treated once daily with ultrasound according to the standard protocol; 75% of the treatments were given by the same operators. The ultrasound device had 20 codes randomly divided over the two treatment options, active or sham, and active and sham use could not be distinguished except by deliberately testing for active ultrasonic production.

Again there was comparability between the groups (88 patients randomised between the two treatments). There was no difference between the groups in any of the ulcer healing parameters studied.

Conclusion

These studies show conclusively that large doses of vitamin C and ultrasound are not effective in promoting ulcer healing. These are good, solid negative results which should not require further investigation. Neither should be purchased for pressure sore management or prevention.

Reference:

G ter Riet, AGH Kessels, P Knipschild. Vitamin C and ultrasound in the treatment of pressure ulcers. Cip-data Koninklijke Bibliotheek, Den Haag. ISBN 90-74130-11-9.

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DRUG MISUSE AND SOCIAL COST

The debate about illicit drugs is set to run and run. There are many voices calling for drug legalisation, and more equally vociferously opposed. These arguments all too often rely upon concepts of freedom of the individual compared with protection of society, and rarely is evidence of harm or lack of harm brought forward as arguments on either side.

The biggest problem for those wishing to use evidence is the paucity of good research.

Reinstating the British System

John Marks, a psychiatrist from Cheshire and Merseyside, has long campaigned for the prescription of heroin for addicts (the British System) [1]. He does not call for wholesale legalisation. Rather he makes the point that to afford black market prices, addicts buy more than they need, adulterate it, and sell the extra to finance their own habits.

This results in a gigantic pyramid selling system in which the major input of cash comes from criminal activity. Where drug abuse is prevalent the proportion of criminal activity ascribed to drugs is seldom lower than 50% and may be 80%.

Thus a heroin habit of one gram per day costing £50 amounts to £15,000 a year. Marks comments that the total amount stolen to support the habit of the estimated 100,000 addicts in the UK is as much as £1.5 billion. This may be a serious underestimate - a car radio with a retail price of £100 is unlikely to raise even 20% of that for the criminal. The retail value of the amount needed to be stolen to support the heroin habit of 100,000 addicts could easily be £7.5 billion or more.

The British system involved addicts getting a ration of their drug of addiction from a GP, and in 1967 when this ended, there were 659 notified addicts, compared with the 100,000 estimated now. In Widnes, Merseyside, where the system continues to operate, there is no infection from HIV, no drug-related deaths and a 96% reduction in acquisitive crime [2].

Even more interesting is a 92% reduction in the incidence of addiction.

These are dramatic claims. While not obtained from RCTs, they are certainly worth further detailed attention.

Drugs and driving

Road accidents are a major cause of preventable deaths in younger age groups. Driving under the influence of intoxicating drugs other than alcohol may be an important cause of traffic injuries. Just how important it is in Memphis, Tennessee (population 690,000) has been highlighted by a detailed report in the New England Journal of Medicine [3].

Motorists stopped for careless driving in the USA usually undergo standard field sobriety tests to assess balance and the ability to follow simple instructions, and these, as well as smell of alcohol, can be used as the basis of an arrest. This study did not look at drivers who were primarily suspected of driving under the influence of alcohol, but rather those in whom there was some impairment but no overt alcohol use.

These drivers were referred to a mobile 'drug van' (a converted ambulance), where the sobriety tests were repeated and videotaped, and where they were asked to supply a urine sample in a special toilet (possible under Tennessee law), and where the urine sample could be tested for cocaine and marijuana metabolites using a field immunoassay system.

All the drivers had been stopped for reckless driving - more than 20 mph over the speed limit, driving on the wrong side of the road, at high speed through red lights or stop signs, at night without lights, or passing dangerously.

In 46 nights 175 subjects were stopped; 97% were men, predominantly in their late teens to early 30s. Moderate or extreme intoxication was shown by 68%.

Urine samples were obtained from 150, and the results are shown in the figure. Marijuana or cocaine metabolites, or both, were detected at levels of 100 ng/mL or 300 ng/mL, respectively, in 14% of those who had only mild signs of intoxication, compared with 85% in those with moderate or extreme intoxication. Overall, 59% of those tested were positive for these drugs.

The most important comparison given in the paper was that during the period of the study there were 111 arrests for driving under the influence of drugs compared with only six in a comparable period in the previous year - and five of those followed serious accidents.

Every so often one comes across a book, monograph or paper that makes a big impression. Perhaps its the result - cure for previously incurable disease - or the method, or just the way it's written. Whatever the reason it is a paper to take to a desert island (Oxford Textbook of Medicine and a work of theology being assumed).

Bandolier wants to start a regular feature of Desert Island Texts, and editor's privilege rules.

Archie Cochrane's little book

I never knew Archie Cochrane, who gave his name and ideas to the Cochrane Centre in Oxford and the Cochrane Collaboration. I think I would have liked him, not only because of a shared background in Welsh mining valleys and along the coast between Barry and Rhose, where he lived, but because this was a man who could think the unthinkable, question the unquestionable and be thoroughly interesting.

His book, the one I would take to my desert island, is called *Effectiveness and Efficiency: random reflections on health services*. It is probably out of print now (though reprinted a few years ago), but worth stirring up a librarian to get from the shelves.

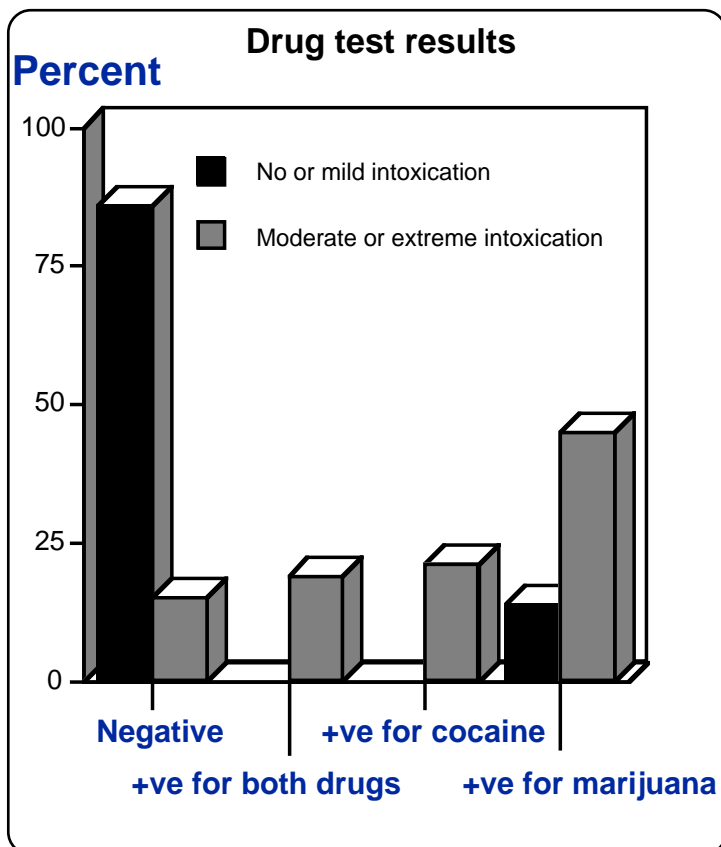
Though barely 100 pages in length and written originally over 20 years ago, it still encapsulates the most important issues in healthcare today - effectiveness, efficiency and care. It is also apolitical: both sides of the political spectrum will find sections to cheer, and other sections which make them think, and perhaps question their thinking. The reason for that is Cochrane's absolute dictum that what's best is what is shown to work.

The basis of the thinking is that randomised controlled trials are the best way of determining what works, and not just in selected therapies like medicines, but in diagnosis, medical devices and management - it sounds modern today, and was a bit revolutionary in the '60s.

There are fascinating chapters on the NHS and its growth during the first 20 years or so after 1948; Cochrane makes the point that it actually had no spending at all on operational research for many years after its birth. I think he would be cheered by the knowledge that the NHS now had an R&D Directorate, but perhaps unhappy that more resources were not being pumped into it.

The chapters on the evaluation of evidence, and on evidence and effectiveness are as fresh now as they were when they were written. *Reflections* is a chapter of what the future of the NHS would be like; accurate in parts, like the numbers of beds falling rapidly in a more intensive service, and perhaps not quite accurate in the prediction that the services of the pathologist would be replaced by experts in effectiveness and efficiency, though that is certainly the direction where public health medicine is headed.

Most important of all is that this book, (written during the tenure of a Rock Carling Fellowship, and originally pub-



This was not a study of incidence, but is usual with drug-related incidence studies, objective testing almost always reveals a much higher incidence than previously thought.

It is common for individuals, whether in medicine, education or government, to deny that drug problems exist. Unless that judgement is backed with objective testing, such information is worthless.

The study also highlights a key part of the legalisation debate which has received little attention. Unlike alcohol, psychoactive compounds like cannabinoids can remain in the body for very long periods, and have lingering effects long after the primary 'high' has disappeared. So driving, or working, or even being at home with impaired judgement can affect the lives of others. Freeing up drug use is likely to mean tightening up on testing.

References:

- 1 J Marks. Drug misuse and social cost. *British Journal of Hospital Medicine* 1994 52: 65-6.
- 2 J Marks. The north wind and the sun. *Proceedings of the Royal College of Physicians of Edinburgh* 1991 21: 319-27.
- 3 D Brookoff, CS Cook, C Williams, CS Mann. Testing reckless drivers for cocaine and marijuana. *New England Journal of Medicine* 1994 331: 518-22.

lished by the Nuffield Provincial Hospitals Trust) retains immense freshness. It's as if Archie Cochrane was talking with you by the fireside after a good dinner: just what you'd need on a desert island.

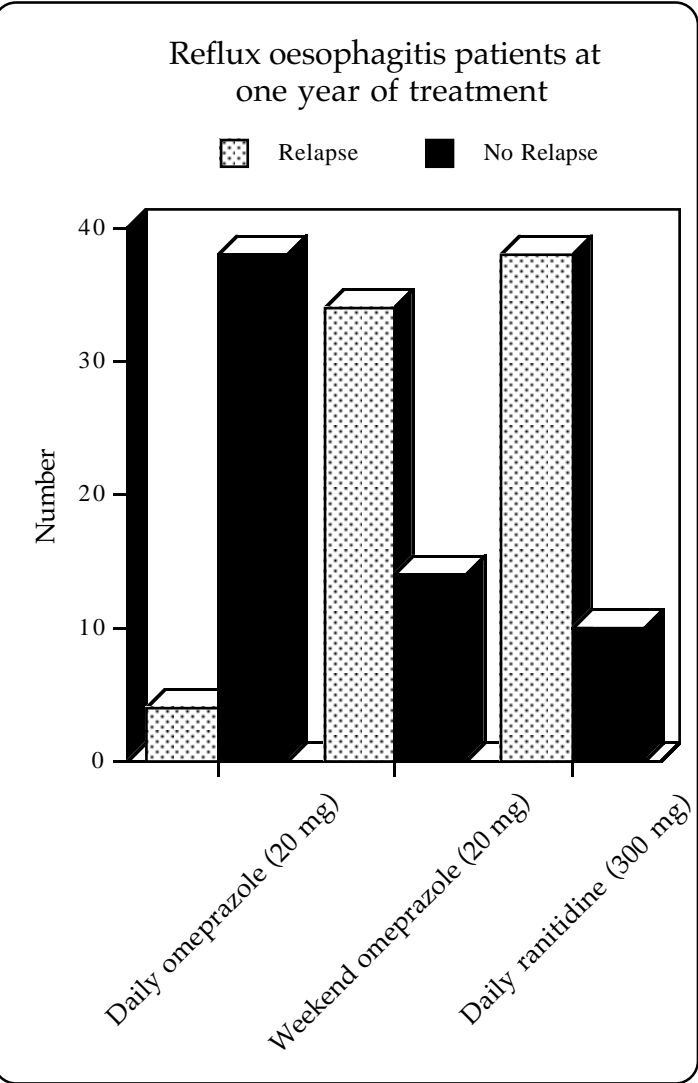
Andrew Moore, Editor

AL Cochrane. Effectiveness and Efficiency. Random Reflections on Health Services. British Medical Journal & Nuffield Provincial Hospitals Trust, Cambridge University Press 1989. [ISBN 0 7279 0282 2].

PREVENTING RELAPSE IN REFLUX OESOPHAGITIS

The expectation has been that healing active oesophagitis would produce a lasting remission by interrupting the vicious cycle of events where the oesophagitis further impairs the acid-reflux mechanism. Unfortunately most patients suffer relapse within a few weeks of stopping acid-suppressant treatment.

So if patients need to take long term treatment, which is best?



Best long-term treatment?

A recent randomised double-blind study in Gut sought to answer that. Patients with oesophagitis were treated with omeprazole, and only those with healing entered the RCT. Treatments were either daily omeprazole (20 mg every morning), omeprazole 20 mg every *weekend* morning (three days a week), or ranitidine 150 mg twice daily.

There were over 50 patients in each group, and they were assessed for relapse by endoscopy (with gastric biopsy) at 6 and 12 months or in the event of symptom recurrence. Histopathology was graded blind at the end of the study and all three groups had similar demographics at randomisation.

There were many analyses in the complex study which involved histopathology as well as laboratory investigations. The simple result was that patients taking daily omeprazole had significantly fewer relapses than those taking omeprazole at weekends, or those taking daily ranitidine. The figures at 12 months (censored for drop-outs) are shown below.

They show that after one year of treatment 89% of those taking daily omeprazole were free of oesophagitis, compared with 32% taking weekend omeprazole and 25% of those taking daily ranitidine.

Reference:

J Dent, ND Yeomans, M Mackinnon, W Reed, FM Narielvala, DJ Hetzel, E Solcia, DJC Shearman. Omeprazole v ranitidine for prevention of relapse in reflux oesophagitis. A controlled double blind trial of their efficacy and safety. Gut 1994 35: 590-8.